Remarks

Applicants have carefully considered the Examiner's Action, and respectfully request reconsideration of this Application in view of the foregoing amendments, and the following remarks.

Claims 1-7, 9-11, 20, 27-36 are pending. Claim 1 is amended as shown, to rearrange the existing text of the claim. The added term "hollow-core" with regard to a plurality of the fibers of the claimed composite is supported at least by paragraphs [0031], FIG 2B, [0046], [0051], [0055], etc.

Claims 32-36 are cancelled in light of the Examiner's finding that the subject matter of those claims fails outside of the presently elected invention I and species (i) made in the reply filed on May 2, 2008. This cancellation is made, however, with the proviso that non-elected species may be pursued in a continuation or divisional application. No new matter has been added.

The specification is amended to change the reference in paragraphs [0016] and [0056] from co-author Stucky to properly reference the lead author, Schacht *et al.,* in *Science* 273(8/9):768-771 (1996). The journal, volume, pages and date are unchanged. Thus, no new matter is added.

Since the Examiner has stated that rejections not reiterated from the previous action are hereby withdrawn, Applicants assume that the Amendment of the Drawings filed with the Previous Response of October 1, 2008 is accepted. Moreover, Applicants appreciate the Examiner's withdrawal of the previous rejections under rejection under § 112, second paragraph, under 35 U.S.C. § 102(b) as being anticipated by Ahola *et al.* and by Bellantone *et al.*, and under 35 U.S.C. § 103(a) of claims 2-3 over Ahola *et al.*, in view of Hench *et al.*, of claim 4 over Ahola, in view of Hench, and further in view of Li *et al*, and over Bellantone in view of Li, and of claims 9 and 10 over Ahola and/or Bellantone, in view of Beaver *et al.*, and further in view of Slivka.

Response to First Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-7, 9-11, 20, and 28-29 under 35 U.S.C. § 103(a) as being obvious over Shvets *et al., Theor. Exper, Chem.* 37(2):1112-115 (2001) and/or Schacht *et al., Science* 273(8/9):768-771 (1996) and Bellantone *et al.* (US 6,482,444). In making this rejection, the Examiner relies upon Shvets as teaching fiber formation in silica in an acid

medium, starting with tetraethyl orthosilicate (TEOS) or tetrabutyl orthosilicate (TBOS), cetyltrimethylammonium bromide (CTMABr) or cetyltrimethylammonium chloride (CTMACl) and HCl. The Examiner relies upon Schacht as teaching silica fibers formed from a material synonymous with TEOS, and suggesting that the "hollow spheres" could be used for drug delivery. However, while the Examiner agrees that neither Shvets nor Schacht teaches the specific limitations of Applicants' claimed invention, she argues that since the fibers are formed by what is alleged to be an "almost identical method" and "all of the same ingredients are utilized," that the "properties of the fibrous preform" of Applicants claimed invention are also the properties of the Shvets' fibers. Specifically, the Examiner points out that both Shvets and Schacht fail to teach a fibrous composite that comprises biodegradable polymers, or a bioactive agent or delivery of a bioactive agent. The Examiner further cites Bellantone for disclosing a bioactive, biodegradable composite material comprising a fibrous composite of oxides and biodegradable polymers, wherein fibers of the composite comprise oxide materials with nano-sized pores. Combining Shvets for the process of forming silica fibers, Schacht for suggesting the use of hollow spheres for drug delivery, and Bellantone for using fibrous composites of oxides for controlled release systems, the Examiner has asserted obviousness of Applicants' claimed invention. However, for the reasons discussed below, Applicants traverse the rejection.

Schacht *et al.,* (*Science* 1996) was explicitly cited in Applicants' application, but under the name of co-author "Stucky *et al.*" See, paragraphs [0016] and [0056]. For clarity purposes, the citation is presently amended in Applicants' specification. Shvets work was predated by similar work cited in their references, *e.g.*, Ozin, Kresge *et al.*, (their references 1, 4, 5, 7 and others.) Similar though not identical references from the same laboratory group were cited in Applicants' application, see paragraphs [0016] and [0017]. Shvets' teaching may, therefore, be considered to be implied by the teaching of Schacht.

There are, however, several significant differences between the materials taught by Shvets and Schacht and those of the present invention:

(a) "Hollow fibers" are present in the material of Applicants' invention, see Figure 2, whereas only hollow spheres, not hollow fibers, were present in Schacht's materials. See, Schacht at 769, middle column, explaining that with stirring, the entire new material comprises "hollow *spherelike* particles are formed until the fiber morphology disappears completely," and in the third column of page 769, "samples, consisting entirely of such *spherical* particles."

Accordingly, Schacht not only teaches only hollow "spheres" – not hollow fibers – but the authors further differentiate between the two morphologies and teach how to eliminate any remaining fibers. While Schacht explains that the Schacht hollow spheres may aggregate into fibers, steps are taken to avoid such aggregates. The Schacht fiber aggregates do not have hollow cores. See description of Schacht's brittle hollow spheres at Applicants' paragraph [0016].

Schacht's hollow spheres have no significance in the rheology of Applicants' fibrous composites since the hollow-cores of the spheres do not communicate with each other. In marked comparison, the hollow cores of Applicants' fibers are important in that the fibrous preform comprises pores in an "interconnecting-porous configuration," (see, express element of claim 1), thereby allowing fluid to rapidly enter and drain. Applicants' fibers may be easily soaked and drained (see paragraph [0050]), unlike many nanocomposites that are difficult to use because the frictional resistance of nano channels to fluid flow is very high. Thus, Applicants' invention, "having a fibrous preform comprising pores in an interconnecting-porous configuration," facilitates substance formation (for example, hydroxyapatite, as Applicants have illustrated in Fig. 5 and 6), and bone growth. Consequently, contrary to the Examiner's apparent assumption, and regardless of any suggestion in the final paragraph of the paper that using the hollow spheres could *possibly* offer a "controlled drug delivery system," neither Schacht nor Shvets (nor a combination of the two) mentions, nor implies, any formation of any hollow fiber or a plurality of fibers self-assembled as a fibrous preform comprising pores in an interconnecting-porous configuration

(b) As stated by Schacht at page 769, column 3, and as referenced in Applicants' paragraph [0016] Schacht's materials were brittle, and could be crushed with a spatula or even during drying ("most popped open during the drying and calcinations steps"). See caption of Schacht's Fig. 2, and paragraph describing Fig. 2. As Applicants have stated in the application at paragraph [0016], "the brittle nature of the spheres in combination with the fact that they were not porous throughout their interior were unfavorable characteristics for use as a matrix." By comparison, Applicants' bioactive, biodegradable fibrous composite of gel-like oxides materials and biodegradable polymers is ductile and can be easily handled, comprising a plurality of fibers self-assembled as a fibrous preform comprising pores in an interconnecting-porous configuration. See the reference to the "conductive" embodiment of Applicants' invention at

paragraph [0042]. The ductile nature of Applicants' invention is partially due to the polymer lips shown in Fig. 4 and mentioned in paragraph [0033].

Thus, the combined prior art offers no teaching or suggestion for how to obtain or form hollow fibers, let alone how to produce hollow-core fibers having the useful, ductile, and easily handled characteristics of Applicants' invention. Although similar starting material chemistry may be used, important differences were introduced by Applicants over the prior art, as disclosed, to result in the formation of hollow fiber preforms. These differences are at least two-fold. First the materials were selected to provide longer chain precursors, *e.g.*, TBOS rather than TEOS, to results in slower reaction rates. Secondly, Applicants used no organic solvent in the formation of an oil phase. By comparison, in the cited combined prior art precursors, such as TEOS, was dissolved in an organic solvent (for example, mesitylene, see first paragraph of p. 769 of Schacht *et al.*) to constitute an oil phase, which then reacts with the water phase to obtain the final product. In contrast, in Applicants' method, TBOS forms the oil phase itself and no other organic solvent was added ("self-assembled as a fibrous preform"). Applicants' use of the term "self-assembled" expressly states that no additional solvent, such as an organic solvent, needs to be added. Notably, TBOS is more oily (hydrophobic) than TEOS.

Applicants' production of "self-assembled" hollow fibers (see, express limitation in claim 1) is, therefore, unexpected and non-obvious over the prior art. Although in both Applicants' claimed method and the prior art, some hollow or solid silica spheres may result from the production process, the presently claimed invention is drawn entirely to the expressly defined fibers – not to the small, spheres that may result as an artifact. Consequently, Applicants' claimed invention is entirely different from Shvets or Schacht in any combination, since neither teaches a "*fibrous*" composite.

Nevertheless, to fill any gaps in the prior art, the Examiner has further added Bellantone to the cited combined references. Bellantone teaches silver-containing bioactive-glass composites prepared by a sol-gel method. (See, Bellantone col. 2, lines 50-55 and col. 4, lines 30-35.) Thus, the fibers of the Bellantone composite are *not a self-assembled* fibrous *preform*, as required by Applicants' claim 1. Rather, Bellantone's mesh, fabric (woven or non-woven), mats, and three-dimensional structures all require an additional assembly of individual fibers produced by a previous separate step. (See Bellantone, 7, line 8, 17, 20, 23.). For example, in one

embodiment, the Bellantone fibers are woven into mats or other structures. (See Bellantone, 7, line 20).

In the prior art, materials either have fast transport (requiring macro or mesopores) or have high surface area (requiring nanopores), but until Applicants' invention, it has never been possible to obtain both by a self assembly process. The prior art teaches that one can achieve a combination of fast transport and high surface area if one uses nanoporous fibers as a starting material, then manually weave the together into a composite. But such an post-formulation assembly method is entirely different from Applicants' "*self-assembly*" method to produce the fibrous preform. And in fact, Applicants' method is a significant improvement to the prior art woven methods.

Moreover, while the Examiner cites Bellantone for teaching a fibrous composite having mesopores and macropores, nowhere does Bellantone teach an "*interconnected multi-porous network configuration*" as defined in the invention of Applicants' claim 1. See Applicants' paragraph [0046]. By comparison, Bellantone, at col. 6, lines 35 -40, describes the post-formation steps that may be taken to adjust the pore volume of the already-formed composite. Thus, any additional pore size or structure in the Bellantone composite, other than nanopores, is necessarily created by a post-formation modification, that requires addition processing, such as sintering and/or foam processes. (See Bellantone, col 6, lines 38-39.) Post processing additions are not an element of Applicants' "fibrous preform."

Consequently, even when the fibers of Bellantone are combined with the brittle, non-interconnected, hollow sphere teaching of Shvets and/or Schacht, the combination does not, and cannot, render obvious Applicants' claimed invention. No element provided by the combination offers a "*self-assembled* multi-porous *fibrous* composite *preform*" of Applicants' claimed invention, requiring no post-formation assembly or modification. As a result, since each and every element of the invention of Applicants' claims 1-7, 9-11, 20, and 28-29 is not disclosed, nor even suggested, by the cited combination of references including Bellantone, Applicants respectfully assert that under the law, these claims cannot be shown to be obvious over the cited combination under 35 U.S.C. §103(a). Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn, and that these claims be moved to allowance.

Applicants have responded to every point in the Examiner's rejection under this heading, but Applicants ask for clarification from the Examiner regarding the reason at page 6 of the

Action, second paragraph for rejecting claim 31. Claim 31 is not within the range of claims identified in the rejection – specifically stated by the Examiner to be claims 1-7, 9-11, 20, and 28-29. Therefore, Applicants have not responded in this section to the Examiner's reasoning for rejecting claim 31, but they will do so if that claim is expressly rejected.

Response to Second Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claims 27 and 30 under 35 U.S.C. § 103(a) as being obvious over Shvets *et al., Theor. Exper, Chem.* 37(2):1112-115 (2001) and/or Schacht *et al., Science* 273(8/9):768-771 (1996) and Bellantone *et al.* (US 6,482,444), and further in view of Aloha *et al.* (WO 97/45367). In making this rejection, the Examiner relies upon the arguments made regarding the First Rejection under 35 U.S.C. § 103(a), above. Further, the Examiner states at page 7 of the Action, that "Shvets/Schacht/Bellantone teach all of the limitations of claims 20 and 11 upon which claims 27 and 30 depend, but fail to teach the limitations further recited by claims 27 and 30." Consequently, to fill that gap, the Examiner has added Ahola.

Notably, however, the Examiner has made no rejection of claims 20 or 11 in this rejection. In the subsequent separate paragraphs of the Action at pages 7 and 8, the Examiner has explained the reasoning behind Ahola's teaching with regard to Applicants' claims 1 and 5, 6 and 11, 7 and 20 and 21, respectively. However, since the Examiner has made no rejection of claims 1, 5, 6, 7, 11, 20 or 21 under Shvets/Schacht/Bellantone/Ahola in this present rejection of claims 27 and 30, Applicants cannot respond to the Examiner's comments.

Regarding claims 27 and 30, Applicants traverse the Examiner's conclusion that Applicants' claimed invention is obvious.

With regard to claims 27 and 30, Ahola teaches a dissolvable silica-xerogel prepared via a sol-gel process. More specifically, Ahola teaches a xerogel composite by spray-drying or sol-spinning methods. (See Ahola, page 9, lines 5 – 35.) Thus, the Ahola composite is not, and cannot be, considered to be "self-assembled." Ahola's configurations, specifically, woven or non-woven mats, filters, and fiber-mats, all require additional assembly of silica-xerogel fibers that were previously produced in a separate step. (See Ahola, page 10, line 1, 13, and 16.). Thus, if the prior art composite resulting from Ahola alone or from the cited combined references all require "post-formulation assembly" – they cannot by definition be "self-assembled." As a result, such composites requiring post-formulation modification or assembly cannot render

obvious Applicants' independent claim 1, nor dependent claims 20 or 29, nor the presently cited claims 27 and 30 in which the "animal is a human."

The cited references in combination cannot teach or suggest more than their various parts. Moreover, as indicated above, while the prior art teaches either fast transport (requiring macro or mesopores) or high surface area (requiring nanopores), the combined prior art has never been able to provide both limitations together – and never by a "self assembly" process. The prior art teaches that one can achieve a combination of fast transport and high surface area, but only if one uses nanoporous fibers as a starting material, and then manually weaves the materials together into a composite. But such an assembly method is entirely different from Applicants' "*self-assembly*" method for providing the fibrous perform. In fact, Applicants' method is a significant improvement to the prior art woven methods.

Moreover, nowhere in the combined cited art is there a teaching of an "*interconnected multi-porous network configuration*" in a self-assembled fibrous perform, as claimed by Applicants without post-formation modifications that require addition processing, such as sintering and/or foam processes.

Consequently, even when the fibers of Bellantone are combined with the brittle, non-interconnected, hollow sphere teaching of Shvets and/or Schacht, and Ahola's drug or therapeutic composition administration to an animal or human, the combination does not, and cannot, render obvious Applicants' claimed invention. No element provided by the combination offers a "*self-assembled* multi-porous *fibrous* composite *preform*" of Applicants' claimed invention, requiring no post-formation assembly or modification. As a result, since each and every element of the invention of Applicants' rejected claims 27 and 30 are not disclosed, nor even suggested by the cited Shvets/Schacht/Bellantone/Ahola combined references, Applicants' claims 27 and 30 are not obvious over the cited combination under 35 U.S.C. §103(a). Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn, and that these claims be moved to allowance.

If the Examiner's rejection, combining Shvets/Schacht/Bellantone/Ahola, were to be applied to pending claims 1-7, 9-11, 20, 28-29 and 31, some of which are mentioned, but none of which are presently rejected by the Examiner, the same reasoning would apply. The cited combination of references fails to teach every element of Applicants' independent claim 1, requiring a "fibrous composite comprising: a plurality of *hollow-core fibers self-assembled as a*

fibrous preform comprising pores in an *interconnecting-porous configuration*," specifically wherein the interconnected pore network comprises pores ranging from nanopores, to mesopores, to macropores. Such a fibrous preform is not possible in the combined prior art because each cited reference in the combination requires specific steps either pre- or post-formation that would preclude the formation of Applicants' preform. See foregoing arguments.

Applicants' claimed invention, however, requires no additional processing steps, such as sintering and/or foam processes to achieve a networked multi-porous fibrous configuration. To the contrary, without the need for any additional steps or processes, Applicants' fibers self-assemble into an interconnected-porous configuration, or preform, as exemplified at Applicants' Example 1, which details initial formation of silica fibers within an emulsion comprised of cationic and anionic materials. (See Applicants' Example 1: Method of Preparing and Testing Fibrous Silica Composites.). As a result, the cited combined references not only fail to render Applicants' claim 1 obvious, but the combination also fails to renders any claim directly or indirectly dependent thereon obvious, whether administered to an animal or human or not. Consequently, Applicants respectfully request that under 35 U.S.C. §103(a), all pending claims be reconsidered, whether expressly rejected or not, and moved to allowance.

In conclusion, Applicants respectfully submit that in light of this present Response and Applicants' comments on record, each rejection of the claims has been overcome, and the claims are now in condition for allowance. Reconsideration and allowance of the pending claims are respectfully requested at the earliest possible date, and Applicants earnestly solicit a Notice of Allowance. Should the Examiner wish to discuss Applicants' Response, she is asked to please

contact Applicants' undersigned representative at the number provided below. If additional fees are due, the Office is authorized to withdraw the necessary amount from Deposit Account 50-4764.

Respectfully submitted,

Date: September 10, 2009

Evelyn H. McConathy
Registration No. 35,279
MONTGOMERY, McCRACKEN,
WALKER & RHOADS, LLP
123 South Broad Street
Philadelphia, PA 19109-1099
Tel: (215) 772.7550
Fax: (215) 772.7620